

### **REMARKS**

In the office action, claims 9 and 15-21 continue to be rejected under §103. In response, the following remarks have been put forth. Claims 9 and 15-21 are pending in the application.

#### **The Invention**

The present invention is a composition *consisting essentially of* gamma vinyl GABA and vitamin B6. The basic and novel characteristics of the claims are 'gamma vinyl GABA' and 'vitamin B6'.

It is known that gamma vinyl GABA (GVG) is involved in several chemical reactions in the brain. For example, on page 5, lines 7-9, the inventors discuss some of these reactions. The effect that GVG has on the many chemical reactions of the brain is highly influenced by the presence of other compounds. For this reason, Applicant used the transitional phrase "consisting essentially of" in the claims. The addition of compounds, other than GVG and vitamin B6, to the claimed composition, would constitute a material change to the basic and novel characteristics of the invention.

#### **35 U.S.C. §103 Rejections**

Claims 9 and 15 continue to be rejected under §103(a) as being unpatentable over Seiler et al. (U.S. Patent No. 4,540,582) in view of Evans et al. (U.S. Patent Application No. 2002/0048612A1). According to the Examiner, Seiler et al. disclose controlling seizures by administering GVG (50mg/kg to 750mg/kg) and glycine, sarcosine or N,N-dimethyl-glycine or a C<sub>1</sub>-C<sub>8</sub> alkyl ester thereof.

The Examiner contends that the broadest interpretation of the claimed range (about 100 to 300 mg/kg) of GVG overlaps with the range disclosed in Seiler et al. The Examiner

recognizes that Seiler et al. do not teach a composition consisting essentially of GVG and vitamin B6.

However, according to the Examiner, Evans et al. disclose compositions containing one or more butyrates and one or more optional ingredients such as antioxidants, antidepressants, memory promoters/enhancers, various vitamins, nutritional and herbal supplements. The Examiner contends that Evans et al. disclose a composition comprising vitamin B6 (0-40mg), L-glutamine, magnesium butyrate and other ingredients. According to the Examiner, the amount of vitamin B6 disclosed in Evans et al. (0-40mg) overlaps with the claimed amount (about 50 to 100mg/day). The Examiner proposes that because Evans et al. allegedly disclose that transformation to GABA is enhanced when butyrates are formulated with promoters including pyridoxine 5-phosphate (vitamin B6), it would have been obvious to one of skill in the art to combine Seiler et al. and Evans et al. and arrive at the claimed invention. Applicants continue to respectfully disagree.

GVG is not a substrate for GABA. GVG is a selective enzyme activated irreversible inhibitor of GABA-transaminase (the enzyme that catabolizes GABA). This definition has been taken directly from Seiler et al. See col. 1, lines 35-39.

A careful reading of Evans et al. reveals that the disclosed composition requires a substrate for GABA, or worded slightly differently, a butyrate that is a substrate for GABA. See, for example, paragraphs [0010] and [0011] of the published application.

Evans et al. provide plenty of examples of such substrates for GABA. See, for example, paragraphs [0012], [0013], and [0015] of the published application. GVG is not mentioned because GVG is not a substrate for GABA. Evans et al. simply do not contemplate or suggest the use of GVG.

Evans et al. do not disclose, hint or suggest using a component other than a substrate for GABA as defined in the specification, in their invention. Therefore, Applicant fails to appreciate how one of ordinary skill in the art would read Evans et al. (methods for treating cognitive and emotional disorders) and be motivated to look to Seiler et al. (methods for treating seizure disorders) for the idea to use GVG, a selective enzyme activated irreversible inhibitor of GABA-transaminase, in a method that requires a substrate for GABA.

Blum et al. is relied on by the Examiner as allegedly teaching that vitamin B6 is an important co-factor in the synthesis of dopamine, serotonin and GABA. There is no disclosure or suggestion in Blum et al. of a composition consisting essentially of GVG and vitamin B6.

The Examiner relies on KSR as evidence that a specific teaching, suggestion or motivation is not required to support a finding of obviousness. However, this does not mean that there need not be some level of teaching, suggestion or motivation demonstrated. In fact, in an internal memo to USPTO technology art unit directors dated May 3, 2007, Margaret Focarino, Deputy Commissioner of Operations at the USPTO stated "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner disclosed." A copy of said memo is attached hereto for the Examiner's convenience.

### **Previous Arguments**

Applicant previously argued that "butyrates" as disclosed and described by Evans et al. do not include GVG. Gamma vinyl GABA (GVG) is not a "substrate for gamma amino butyric acid (GABA)...the substrate transformed into GABA within the brain." GVG is an irreversible inhibitor of GABA-transaminase, the enzyme that catabolizes GABA.

In response, the Examiner points to the specification's definition of a GABAergic drug as being any compound that potentiates the GABAergic system or increases GABA levels in the CNS. However, the claims are limited to a particular compound, GVG. GVG causes an increase

in GABA in the CNS indirectly by inhibiting the enzyme that breaks down GABA. GVG is not a substrate for GABA. The specification clearly acknowledges the difference between GVG and the other GABAergic drugs disclosed. See, for example, paragraphs [0006], [0021] and [0023].

Applicant previously argued that Evans et al. disclose the possibility of hundreds of combinations of butyrates and optional ingredients. Evans et al. does not specifically disclose or suggest the claimed composition that consists essentially of GVG and vitamin B6.

The Examiner responded to the above by stating that the “exemplified composition does not “list hundreds” of optional ingredients as Applicant contends. Applicant did not intend to suggest that Evans et al. list hundreds of optional ingredients. Rather, Applicant’s intent was to assert that Evans et al. disclose several examples of possible butyrates and several examples of possible optional ingredients which results in a large number, perhaps not quite one hundred, possible compositions.

Applicant fails to appreciate how a person of ordinary skill in the art would read Evans et al. and Seiler et al. and arrive at a composition consisting essentially of GVG and vitamin B6 – especially when GVG is not disclosed by Evans et al. Evans et al. doesn’t even suggest a composition consisting essentially of a GABA substrate and vitamin B6. GVG and magnesium butyrate are not interchangeable. GVG and L-glutamine are not interchangeable. GVG is not a GABA substrate.

As additional support for Applicant’s assertion that GVG is not a GABA substrate or a butyrate as defined by Evans et al., a declaration by Dr. Charles Ashby is hereby submitted. Dr. Ashby’s expertise is in the pharmaceutical sciences. In paragraph 7 of the declaration, Dr. Ashby explains that GVG is not an equivalent of, or interchangeable with, butyrates as disclosed by Evans, et al.

More importantly, in paragraph 6 of the declaration, Dr. Ashby explains that butyrates, such as magnesium butyrate, are precursors for GABA, but have no effect on GABA levels in the brain because they do not cross the blood-brain barrier. GVG, on the other hand, has a significant effect on GABA levels in the brain because it inhibits GABA degradation (via inhibiting the enzyme that catabolizes GABA - GABA-T).

Moreover, the claimed composition consists essentially of GVG and vitamin B6. As mentioned above, the addition of ingredients other than GVG and vitamin B6 would constitute a material change in the basic and novel characteristics of the claimed invention. It is known that (GVG) is involved in several chemical reactions in the brain. For example, on page 5, lines 7-9, the inventors discuss some of these reactions. The effect that GVG has on the many chemical reactions of the brain is highly influenced by the presence of other compounds. For this reason, Applicant uses the transitional phrase "consisting essentially of" in the claims. The addition of compounds, other than GVG and vitamin B6, to the claimed composition, would constitute a material change to the basic and novel characteristics of the invention.

Applicant has emphasized the importance of the composition consisting essentially of GVG and vitamin B6, and wherein the vitamin B6 is in an amount of about 50 to 100 mg/day. Upon combining Seiler et al. and Evans et al. all of the claim limitations are not taught. Especially in view of the Examiner's erroneous characterization of GVG as a "butyrate" as described by Evans et al.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection under §103 based on Seiler et al. in view of Evans et al.

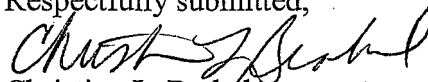
In light of the foregoing remarks and declaration, Applicant respectfully submits that the application is now in condition for allowance. If the Examiner believes a telephone discussion

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with the Applicant's representative would be of assistance, he/she is invited to contact the undersigned at his/her convenience.

Respectfully submitted,



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MEMORANDUM

DATE: May 3, 2007

TO: Technology Center Directors

FROM: *Margaret A. Focarino*  
Margaret A. Focarino  
Deputy Commissioner  
for Patent Operations

SUBJECT: Supreme Court decision on *KSR Int'l. Co., v. Teleflex, Inc.*

The Supreme Court has issued its opinion in *KSR*, regarding the issue of obviousness under 35 U.S.C. § 103(a) when the claim recites a combination of elements of the prior art. *KSR Int'l Co. v. Teleflex, Inc.*, No 04-1350 (U.S. Apr. 30, 2007). A copy of the decision is available at <http://www.supremecourtus.gov/opinions/06pdf/04-1350.pdf>. The Office is studying the opinion and will issue guidance to the patent examining corps in view of the *KSR* decision in the near future. Until the guidance is issued, the following points should be noted:

- (1) The Court reaffirmed the *Graham* factors in the determination of obviousness under 35 U.S.C. § 103(a). The four factual inquiries under *Graham* are:
- (a) determining the scope and contents of the prior art;
  - (b) ascertaining the differences between the prior art and the claims in issue;
  - (c) resolving the level of ordinary skill in the pertinent art; and
  - (d) evaluating evidence of secondary consideration.

*Graham v. John Deere*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966).

- (2) The Court did not totally reject the use of "teaching, suggestion, or motivation" as a factor in the obviousness analysis. Rather, the Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a).

- (3) The Court rejected a rigid application of the "teaching, suggestion, or motivation" (TSM) test, which required a showing of some teaching, suggestion, or motivation in the prior art that would lead one of ordinary skill in the art to combine the prior art elements in the manner claimed in the application or patent before holding the claimed subject matter to be obvious.

(4) The Court noted that the analysis supporting a rejection under 35 U.S.C. § 103(a) should be made explicit, and that it was "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed. The Court specifically stated:

Often, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an **apparent reason** to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis **should be made explicit**.

*KSR*, slip op. at 14 (emphasis added).

Therefore, in formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.